International application No.

PCT/JP2004/004523

| A. CLASSIFIC | CATION OF SUBJECT MATTER 7 C12N15/09, C07K14/47, C12N15 C12N1/21, C12N5/10, C12P21/0 | | | | |
|--|--|--|--|--|--|
| According to Int | According to International Patent Classification (IPC) or to both national classification and IPC | | | | |
| B. FIELDS SE | | | | | |
| Minimum docun Int.Cl | Minimum documentation searched (classification system followed by classification symbols) Int.Cl ⁷ C12N15/09, C07K14/47, C12N15/11, C12N1/15, C12N1/19, C12N1/21, C12N5/10, C12P21/00, A61K38/17, A61P35/00 | | | | |
| | searched other than minimum documentation to the extension | • | | | |
| SwissPı | wase consulted during the international search (name of cot/PIR/Geneseq, WPI/BIOSIS (DIA c/EMBL/DDBJ/Geneseq | | | | |
| C. DOCUMEN | ITS CONSIDERED TO BE RELEVANT | | | | |
| Category* | Citation of document, with indication, where ap | opropriate, of the relevant passages | Relevant to claim No. | | |
| <u>X</u> . <u>Y</u> | J. E. OBLONG. et al., Site-dative site cysteines in huma competitive inhibitors of hur reductase and elimination of of thioredoxin., J.Biol.Chem. No.16, pages 11714 to 11720 | n thioredoxin produces man thioredoxin mitogenic properties | 1-13 $14-16,18$ | | |
| X Y | K. TONISSEN, et al., Site-din human thioredoxin., Identific as critical to its function in pregnancy factor", system., 5 Vol.268, No.30, pages 22485 t | cation of cysteine 74 in the "early J.Biol.Chem., (1993), | 14-13 $14-16$, 18 | | |
| × Further do | cuments are listed in the continuation of Box C. | See patent family annex. | | | |
| "A" document de to be of parti "E" earlier applie filing date "L" document who cited to esta special reason "O" document ref document puthe priority d | pories of cited documents: Iffining the general state of the art which is not considered cular relevance ation or patent but published on or after the international which may throw doubts on priority claim(s) or which is blish the publication date of another citation or other in (as specified) Ferring to an oral disclosure, use, exhibition or other means blished prior to the international filing date but later than ate claimed completion of the international scarch 1, 2004 (21.04.04) | "T" later document published after the interdate and not in conflict with the application the principle or theory underlying the interded after the principle or theory underlying the considered novel or cannot be considered to involve an inventive sombined with one or more other such being obvious to a person skilled in the document member of the same patent for | tion but cited to understand evention laimed invention cannot be lered to involve an inventive laimed invention cannot be latter when the document is documents, such combination art lamily | | |
| | gaddress of the ISA/ e Patent Office | Authorized officer | | | |
| Faccimile No. | | Telephone No. | i | | |

Form PCT/ISA/210 (second sheet) (January 2004)

Form PCT/ISA/210 (continuation of second sheet) (January 2004)

International application No. PCT/JP2004/004523

| | PCT/JP20 | 0047004523 |
|---|--|---|
|). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
| Citation of document, with indication, where appropriate, of the relevant | Relevant to claim No. | |
| of the thioredoxin growth factor system be antitumor 2-imidazolyl disulfides., Bioch | y iem., | 1 <u>1-13</u> 14-16,18 |
| JP 10-191977 A (Oriental Yeast Co., Ltd. 28 July, 1998 (28.07.98), & EP 0853088 A2 |), | $\frac{1-13}{14-16,18}$ |
| thioredoxin increase cell proliferation a dominant-negative mutant thioredoxin reve transformed phenotype of human breast can | nd a rses the cer | 1-16,18 |
| WO 2004/013283 A2 (UNIVERSITY OF ROCHEST) 12 February, 2004 (12.02.04), (Family: none) | ER), | 1-16,18 |
| JP 5-507209 A (Genetics Institute, Inc.) 21 October, 1993 (21.10.93), & WO 92/13955 A1 & US 5270181 A & EP 574506 A1 | | 1-16,18 |
| | | |
| | Citation of document, with indication, where appropriate, of the releve D. L. KIRKPATRICK et al., Mechanisms of it of the thioredoxin growth factor system it antitumor 2-imidazolyl disulfides., Bioch Pharmacol., (1998), Vol.55, No.7, pages 9 JP 10-191977 A (Oriental Yeast Co., Ltd. 28 July, 1998 (28.07.98), EP 0853088 A2 A. GALLEGOS, et al., Transfection with hut thioredoxin increase cell proliferation adominant-negative mutant thioredoxin revetransformed phenotype of human breast can cells., Cancer Res., (1996), Vol.56, No.2 pages 5765 to 5770 WO 2004/013283 A2 (UNIVERSITY OF ROCHEST: 12 February, 2004 (12.02.04), (Family: none) JP 5-507209 A (Genetics Institute, Inc.) 21 October, 1993 (21.10.93), EM WO 92/13955 A1 EM SEP 574506 A1 | Citation of document, with indication, where appropriate, of the relevant passages D. L. KIRKPATRICK et al., Mechanisms of inhibition of the thioredoxin growth factor system by antitumor 2-imidazolyl disulfides., Biochem., Pharmacol., (1998), Vol.55, No.7, pages 987 to 994 JP 10-191977 A (Oriental Yeast Co., Ltd.), 28 July, 1998 (28.07.98), EP 0853088 A2 A. GALLEGOS, et al., Transfection with human thioredoxin increase cell proliferation and a dominant-negative mutant thioredoxin reverses the transformed phenotype of human breast cancer cells., Cancer Res., (1996), Vol.56, No.24, pages 5765 to 5770 WO 2004/013283 A2 (UNIVERSITY OF ROCHESTER), 12 February, 2004 (12.02.04), (Family: none) JP 5-507209 A (Genetics Institute, Inc.), 21 October, 1993 (21.10.93), EVENT OF ROCHESTER), 12 October, 1993 (21.10.93), EVENT OF ROCHESTER), 21 October, 1993 (21.10.93), EVENT OF ROCHESTER), 22 October, 1993 (21.10.93), EVENT OF ROCHESTER), 21 October, 1993 (21.10.93), EVENT OF ROCHESTER) |

International application No.

PCT/JP2004/004523

| Box N | o. I | Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet) |
|-------|-----------------------|--|
| 1. W | ith regar vention, | d to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed the international search was carried out on the basis of: |
| a. | type | of material · |
| | × | a sequence listing |
| | | table(s) related to the sequence listing |
| b. | forms | at of material |
| | | in written format |
| | × | in computer readable form |
| c. | time o | of filing/furnishing |
| | | contained in the international application as filed |
| | × | filed together with the international application in computer readable form |
| | | furnished subsequently to this Authority for the purposes of search |
| 2. × | In add | dition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed |
| | or fur applie | nished, the required statements that the information in the subsequent or additional copies is identical to that in the attended attended to the application as filed, as appropriate, were furnished. |
| 3. Ad | ditional | comments: |
| J. Au | uttional | continents; |
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International application No. PCT/JP2004/004523

| Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet) |
|---|
| This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: 1. X Claims Nos.: 17 because they relate to subject matter not required to be searched by this Authority, namely: Claim 17 pertains to methods for treatment of the human body by therapy and thus relates to a subject matter which this International Searching Authority is not required to search. 2. Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically: |
| 3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). |
| Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet) |
| This International Searching Authority found multiple inventions in this international application, as follows: The matter common to claims 1, 7 to 10 and 13 resides in polypeptides having an amino acid sequence -Cys-Gly-Pro-A (wherein A represents an arbitrary amino acid other than Cys). As the results of the search, it is clarified that the polypeptides having an amino acid sequence -Cys-Gly-Pro-A (wherein A represents an arbitrary amino acid other than Cys) are not novel because of having been disclosed in document "A, GALLEGOS, et. al., Cancer Res. (1996), Vol.56, No.24, p.5765-5770". Thus, this common matter falls within the category of prior art and, therefore, cannot be regarded as a special technical feature in the meaning within PCT Rule 13.2. (Continued to extra sheet.) 1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims. 2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: |
| No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: |
| The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees. |

International application No.

PCT/JP2004/004523

Continuation of Box No.III of continuation of first sheet(2)

Such being the case, there is no special technical matter common to all claims and the above invention groups cannot be considered as a group of inventions so linked as to form a single general inventive concept. However, this authority did not invite payment of any additional fee, since all searchable claims could be searched without effort justifying an additional fee.

Form PCT/ISA/210 (extra sheet) (January 2004)

A. 発明の属する分野の分類(国際特許分類 (IPC))

Int. C1⁷ C12N15/09, C07K14/47, C12N15/11, C12N1/15, C12N1/19, C12N1/21, C12N5/10, C12P21/00, A61K38/17, A61P35/00

B. 調査を行った分野

調査を行った最小限資料(国際特許分類(IPC))

Int. C1⁷ C12N15/09, C07K14/47, C12N15/11, C12N1/15, C12N1/19, C12N1/21, C12N5/10, C12P21/00, A61K38/17, A61P35/00

最小限資料以外の資料で調査を行った分野に含まれるもの

国際調査で使用した電子データベース (データベースの名称、調査に使用した用語)

SwissProt/PIR/Geneseq, WPI/BIOSIS (DIALOG), CA/MEDLINE/WPIDS/BIOSIS (STN), Genbank/EMBL/DDBJ/Geneseq,

| C. | 関連す | ス | と製み | <u>_</u> | カス | 柚か |
|----------|-----|-----|------|----------|-----|-------------|
| \sim . | | ٠., | こっぱい | • | avw | 大服 人 |

| | S C PRO S A VO X RX | |
|-----------------|--|-------------------------|
| 引用文献の カテゴリー* | 引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示 | 関連する 請求の範囲の番号 |
| <u>X</u> Y | J, E, OBLONG, et. al., Site-directed mutagenesis of active site cysteines in human thioredoxin produces competitive inhibitors of human thioredoxin reductase and elimination of mitogenic properties of thioredoxin., J. Biol. Chem. (1994), Vol. 269, No. 16, p. 11714-11720 | $1-13 \\ 14-16,18$ |
| <u>X</u> Y | K, TONISSEN, ey. al., Site-directed mutagenesis of human thioredoxin. Identification of cysteine 74 as critical to its function in the "early pregnancy factor" system., J. Biol. Chem. (1993), Vol. 268, No. 30, p. 22485-22489 | $\frac{1-13}{14-16,18}$ |

区欄の続きにも文献が列挙されている。

パテントファミリーに関する別紙を参照。

* 引用文献のカテゴリー

- 「A」特に関連のある文献ではなく、一般的技術水準を示す もの
- 「E」国際出願日前の出願または特許であるが、国際出願日 以後に公表されたもの
- 「L」優先権主張に疑義を提起する文献又は他の文献の発行 日若しくは他の特別な理由を確立するために引用する 文献(理由を付す)
- 「〇」口頭による開示、使用、展示等に言及する文献
- 「P」国際出願日前で、かつ優先権の主張の基礎となる出願

の日の後に公表された文献

- 「T」国際出願日又は優先日後に公表された文献であって 出願と矛盾するものではなく、発明の原理又は理論 の理解のために引用するもの
- 「X」特に関連のある文献であって、当該文献のみで発明 の新規性又は進歩性がないと考えられるもの
- 「Y」特に関連のある文献であって、当該文献と他の1以 上の文献との、当業者にとって自明である組合せに よって進歩性がないと考えられるもの
- 「&」同一パテントファミリー文献

国際調査を完了した日

21.04.2004

国際調査報告の発送日

11 5. 2004

国際調査機関の名称及びあて先

日本国特許庁 (ISA/JP) 郵便番号100-8915

東京都千代田区霞が関三丁目4番3号

特許庁審査官(権限のある職員) 鈴木 美葉子 4N 3335

電話番号 03-3581-1101 内線 3488

| C (続き). | 関連すると認められる文献 | |
|-------------------------|---|---|
| 引用文献の | | 関連する |
| カテゴリー* <u>X</u> Y | 引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示 D, L, KIRKPATRICK, et. al., Mechanisms of inhibition of the thioredoxin growth factor system by antitumor 2-imidazolyl disulfides., Biochem. Pharmacol. (1998), Vol. 55, No. 7, p. 987-994 | 請求の範囲の番号 <u>1-13</u> 14-16,18 |
| <u>X</u> Y | JP 10-191977 A(オリエンタル酵母工業株式会社)1998.07.28 & EP 0853088 A2 | $ \begin{array}{c c} 1-13 \\ 14-16,18 \end{array} $ |
| х | A, GALLEGOS, et. al., Transfection with human thioredoxin increases cell proliferation and a dominant-negative mutant thioredoxin reverses the transformed phenotype of human breast cancer cells., Cancer Res. (1996), Vol. 56, No. 24, p. 5765-5770 | 1-16, 18 |
| РХ | WO 2004/013283 A2 (UNIVERSITY OF ROCHESTER) 2004.02.12 (ファミリーなし) | 1-16, 18 |
| A | JP 5-507209 A (ジェネティックス・インスティテュート・インコーポレイテッド) 1993.10.21 & WO 92/13955 A1 & US 5270181 A & EP 574506 A1 | 1-16, 18 |
| | | |
| | · | |

| 第1欄 ヌクレオチドン | スはアミノ酸配列 (第1ページの1. bの続き) |
|-----------------------------------|---|
| 1. この国際出願で開え 以下に基づき国際即 | Fされかつ請求の範囲に係る発明に必要なヌクレオチド又はアミノ酸配列に関して、 関査を行った。 |
| a. タイプ | ☑ 配列表 |
| | □ 配列表に関連するテーブル |
| b. フォーマット | 雷 |
| | コンピュータ読み取り可能な形式 |
| c . 提出時期 | 出願時の国際出願に含まれる |
| | 区 この国際出願と共にコンピュータ読み取り可能な形式により提出された |
| | □ 出願後に、調査のために、この国際調査機関に提出された |
| 2. × さらに、配列表 した配列が出願 出があった。 | 又は配列表に関連するテーブルを提出した場合に、出願後に提出した配列若しくは追加して提出 限時に提出した配列と同一である旨、又は、出願時の開示を超える事項を含まない旨の陳述書の提 |
| 3. 補足意見: | |
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| 第Ⅱ欄 請求の範囲の一部の調査ができないときの意見(第1ページの2の続き) |
|---|
| 法第8条第3項 (PCT17条(2)(a)) の規定により、この国際調査報告は次の理由により請求の範囲の一部について作成しなかった。 |
| 1. <a> |
| 請求の範囲17は、人体の治療方法に該当するものであるから、国際調査機関が 調査をすることを要しない対象に係るものである。 |
| 2. □ 請求の範囲は、有意義な国際調査をすることができる程度まで所定の要件を満たしていない国際出願の部分に係るものである。つまり、 |
| |
| 3. |
| 第Ⅲ欄 発明の単一性が欠如しているときの意見(第1ページの3の続き) |
| 次に述べるようにこの国際出願に二以上の発明があるとこの国際調査機関は認めた。 |
| 請求の範囲1、7~10、13に共通の事項は、-Cys-Gly-Pro-A (AはCys以外の任意のアミノ酸を示す)で表されるアミノ酸配列を有するポリペプチドである。しかしながら、調査の結果、-Cys-Gly-Pro-A (AはCys以外の任意のアミノ酸を示す)で表されるアミノ酸配列を有するポリペプチドは、文献「A, GALLEGOS, et. al., Cancer Res. (1996), Vol. 56, No. 24, p. 5765-577 0」に開示されているから、新規でないことが明らかとなった。よって、この共通事項は先行技術の域を出るものではないから、PCT規則13.2における特別な技術事項であるとはいえない。それ故に、請求の範囲の全てに共通の特別な技術事項はなく、上記発明群が単一の一般的な発明概念を形成するように関連している一群の発明であるとは認められない。しかし、追加調査手数料を要求するまでもなく、全ての調査可能な請求の範囲について調査することができたので、追加調査手数料の納付を求めなかった。 |
| 1. 出願人が必要な追加調査手数料をすべて期間内に納付したので、この国際調査報告は、すべての調査可能な請求の範囲について作成した。 |
| 2. × 追加調査手数料を要求するまでもなく、すべての調査可能な請求の範囲について調査することができたので、追加調査手数料の納付を求めなかった。 |
| 3. 出願人が必要な追加調査手数料を一部のみしか期間内に納付しなかったので、この国際調査報告は、手数料の納付のあった次の請求の範囲のみについて作成した。 |
| 4. U 出願人が必要な追加調査手数料を期間内に納付しなかったので、この国際調査報告は、請求の範囲の最初に記載されている発明に係る次の請求の範囲について作成した。 |
| 追加調査手数料の異識の申立てに関する注意 Ш 追加調査手数料の納付と共に出願人から異識申立てがあった。 |
| □ 追加調査手数料の納付と共に出願人から異議申立てがなかった。 |